

**REMARKS**

In response to the Office Action dated April 4, 2006 in connection with the above application, Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants appreciate the Examiner's helpful suggestions during the telephonic interview dated July 6, 2006.

**Double Patenting**

Claims 39, 73, 89, 90, 93, and 95-97 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-16 and 18-24 of U.S. Patent No. 6,887,674 (the '674 patent). Applicants respectfully traverse this rejection.

Specifically, the Examiner asserts that "[t]he specification [of the '674 patent] provides further support for the role of Ephrin B2 expression in smooth muscle cells in the characterization of embryonic development (see working example 7 that discloses a role in smooth muscle cells)." Office Action, page 3, lines 13-15.

Applicants respectfully submit that the Examiner appears to have misunderstood working example 7 of the '674 patent. Contrary to the Examiner's assertion, working example 7 of the '674 patent does **not** describe Ephrin B2 expression or any role of Ephrin B2 in smooth muscle cells. Instead, it teaches that Ephrin B2 (ligand) and EphB4 (receptor) are expressed on endocardial cells which are known to consist of endothelial cells (see, e.g., Paulus WJ, 1994, Cardiovasc Drug Ther. 8:437-46, the abstract is enclosed herewith as **Exhibit A**). Further, one of skill in the art would understand that the '674 patent mentions "smooth muscle cells" in working example 7 merely because of the known interaction between endothelial cells and smooth muscle cells (see, e.g., **Exhibit A**), and not because of any suggestion that Ephrin B2 is expressed in the smooth muscle cells.

By contrast, the present application describes the unexpected finding that ephrinB2 is expressed in arterial smooth muscle cells (see, e.g., working examples 13-15 on pages 52-64). For example, the specification teaches that "[t]he observation of ephrinB2 expression in adult arterial smooth muscle cells was **surprising**, as initial studies of its expression in embryonic arteries had failed to detect it in the smooth muscle layer (Adams, R., *et al.*, *Genes Dev.* 13: 295-306 (1999); Wang, H.U., *et al.*, *Cell* 93:741-753 (1998)) . . ." (see, e.g., page 62, lines 14-29, emphasis added). In light of the teachings of the instant specification and the knowledge in the art at the time this application was filed, a skilled artisan would conclude that the '674 patent neither anticipates nor renders obvious the instant claims.

Further, the Examiner asserts that "the claims of '674 would encompass practicing the instantly claimed methods, and given the guidance of the specification of '674, arterial smooth muscle cells would have been [are] anticipated because of the role in development." Office Action, page 3, lines 16-19.

Applicants have argued above that the '674 patent does not anticipate or render obvious the instant claims, contrary to the Examiner's assertion. The instant claims are explicitly directed to a method for assessing an effect of an agent on arterial smooth muscle cells, whereas the claims of the '674 patent do not relate to a method involving "arterial smooth muscle cells." Applicants contend that the Examiner has improperly read the "arterial smooth muscle cells" into the claims of the '674 patent. Applicants submit that the instant claims are patentably distinct from the claims of the '674 patent. Reconsideration and withdrawal of the double patenting rejection are respectfully requested.

#### Claim Rejections under 35 U.S.C. § 102(f)

Claims 39, 73, 89, 90, 93, and 95-97 are rejected under 35 U.S.C. § 102(f) because Applicant allegedly did not invent the claimed subject matter. Applicants respectfully traverse this rejection.

Specifically, the Examiner asserts that "[t]he methods of '674 encompass the use of any cell, and dependent claims set forth cells of the artery and veins, . . . and support for the role of

Ephrin B2 expression in smooth muscle cells in the characterization of embryonic development (see working examples) . . . the claims of '674 would encompass practicing the instantly claimed methods, and given the guidance of the specification of '674, arterial smooth muscle cells would have been [are] anticipated because of the role in development." Office Action, page 4, lines 19-26.

Applicants have presented arguments above that the instant claims and teachings are patentably distinct from the claims of the '674 patent. Applicants reiterate that the '674 patent does not anticipate or render obvious the instant claims which are directed to a method for assessing an effect of an agent on arterial smooth muscle cells. Applicants contend that the Examiner has improperly read the "arterial smooth muscle cells" into the claims of the '674 patent. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 102(e)

Claims 39, 73, 89, 90, 93, and 95-97 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,887,674 (the '674 patent). Applicants respectfully traverse this rejection.

Specifically, the Examiner asserts that "it appears that '674 demonstrates that expression [of Ephrin B2] was in smooth muscle cells, at the least as evidenced by it[s] role in development demonstrated in Example 7." Office Action, page 5, lines 17-19.

Applicants have argued above that the '674 patent does not anticipate or render obvious the instant claims. The '674 patent does **not** describe Ephrin B2 expression or any role of Ephrin B2 in smooth muscle cells. Instead, it teaches that Ephrin B2 is expressed on endocardial cells which are known to consist of endothelial cells. The '674 patent does not teach or suggest a method of assessing an effect of an agent on arterial smooth muscle cells as recited in the instant claims, thus failing to meet the limitations of independent claim 39. Accordingly, Applicants submit that all claims are not anticipated by the '674 patent.

Further, Applicants reiterate that the present application describes the **unexpected** finding that ephrinB2 is expressed in arterial smooth muscle cells. The '674 patent does not

provide any motivation to modify their methods by using smooth muscle cells. In fact, at the time the '674 patent was filed, arterial smooth muscle cells were not even known to express EphrinB2. Thus, the '674 patent fails to render obvious the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e) are respectfully requested.

### **CONCLUSION**

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this submission, please charge the fees to our **Deposit Account No. 18-1945, under Order No. CTCH-P01-007.**

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Respectfully submitted,

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